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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/865,993	05/25/2001	Brett P. Monia	RTS-0175	5849

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EXAMINER
ZARA, JANE J

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 05/07/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary	Application No. 09/865,993	Applicant(s) Monia et al
	Examiner Jane Zara	Art Unit 1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 20, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 2, 4-10, and 12-15* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 2, 4-10, and 12-15* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 9
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This Office action is in response to the communication filed February 20, 2003, Paper No. 7.

Claims 1, 2, 4-10, 12-15 are pending in the instant application.

Any rejections not repeated in this Office action are hereby withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 12, 13 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, lines 1 and 3, the metes and bounds of the term "compound" cannot be determined. Appropriate clarification is requested.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 4-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ishibashi et al and , in view of the combined teachings of Milner et al and Baracchini et al insofar as the claims are drawn to compositions comprising antisense oligonucleotide compounds between 8-50 nucleotides which specifically target and inhibit the expression of human dual specific phosphatase 5 (DUSP5, a.k.a. B23/hVH-3) of SEQ ID NO: 10 in vitro, and which oligonucleotides further comprise a phosphorothioate internucleotide linkage modification, a 2'-O-methoxyethyl sugar modification, a 5-methyl cytosine nucleobase modification, and may optionally comprise a chimeric oligonucleotide, and which compositions further comprise a pharmaceutically acceptable diluent and a colloidal dispersion system.

Ishabashi et al teach the polynucleotide sequence of DUSP5 encoded by SEQ ID NO: 10 (See especially the abstract on page 29,898 and figure 1 on page 29,899).

Sato et al teach increases in the expression of B23/hVH-3 (DUSP5) as a result of lysophosphatidylcholine in vascular endothelial cells, identifying DUSP5 as a potential mediator in artherogenesis (See especially the abstract and text on page 1119; table 1 on page 1121; figures 2 and 3 on page 1122; and text on page 1125).

Ishibashi et al and Sato et al do not teach the in vitro inhibition of DUSP5 expression using antisense oligonucleotides between 8-50 nucleobases, nor the incorporation of any

modification into the antisense oligonucleotides, nor compositions comprising antisense oligonucleotides and pharmaceutically acceptable diluents or colloidal dispersion systems.

Milner teaches methods of designing and assessing the ability of various antisense oligonucleotides to target and inhibit the expression of a target nucleic acid of known nucleic acid sequence in vitro (See entire document, especially figure 1 on p 538).

Baracchini et al teach the incorporation of phosphorothioate internucleotide linkages, 2'-O-methoxy ethyl sugar modifications, 5 methyl cytosines and chimeric structures into antisense oligonucleotides for enhancing target binding, cellular uptake and stability of antisense oligonucleotides, as well as compositions comprising antisense oligonucleotides, pharmaceutically acceptable diluents and colloidal dispersion systems (see col. 4-14).

It would have been obvious to one of ordinary skill in the art to target and inhibit the expression of DUSP5 in vitro comprising the administration of antisense oligonucleotides between 8-50 nucleobases because Milner teaches methods of designing and assessing antisense oligonucleotides between 8-50 nucleobases for their ability to target and inhibit the expression of a known target gene in vitro, and Ishibashi teaches the nucleic acid sequence encoding DUSP5 (of SEQ ID NO: 10). One of ordinary skill in the art would have been motivated to utilize such a method of finding optimal antisense oligonucleotides between 8-50 nucleobases which best target and inhibit DUSP5 expression in order to study this target molecule's role in various cellular processes such as signal transduction and cell cycle regulation, because Ishibashi teaches the potential involvement of DUSP5 in such cellular processes. One of ordinary skill in the art also

would have been motivated to inhibit the expression of DUSP5 in cells in vitro in order to study DUSP5's molecular involvement in artherogenesis, because Sato et al teach the increase of expression of DUSP5 in conditions of artherogenesis stimulation, and Sato et al teach the motivation to study the participation and orchestration of vascular endothelial cell derived genes and their involvement in such artherogenesis, thrombosis and fibrinolysis (See especially page 1125). One of ordinary skill in the art would have been motivated to incorporate various modifications into antisense such as internucleotide linkage, nucleobase, or sugar modifications, as well as designing chimeric antisense oligonucleotides, because Baracchini had taught previously that such modifications contribute to the stability, cellular uptake and target binding of antisense oligonucleotide compounds. One of ordinary skill in the art therefore would have expected that antisense comprising such modifications would exhibit enhanced stability, cellular uptake and target binding. One of ordinary skill in the art would have been motivated to utilize compositions comprising pharmaceutically acceptable diluents and colloidal dispersion systems, in combination with antisense oligonucleotides, for transfecting target cells because such compositions had been taught previously by Baracchini et al and one would have expected that such compositions would minimize toxic effects of target cells while enhancing cellular uptake of the antisense oligonucleotides. Therefore, the invention has a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Ram R. Shukla

RAM SHUKLA
PRIMARY EXAMINER

JZ

May 4, 2003